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Research Article

SYNTHESIS OF 2, 4-DIHYDROXY SUBSTITUTED CHALCONES USING SILICA SULPHURIC ACID REAGENT UNDER SOLVENT FREE CONDITIONS

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ABSTRACT

A series of α,β-unsaturated ketones derived from 2,4-dihydroxy acetophenone with various substituted benzaldihydes under solvent free condition using silica-sulfuric acid as a reagent in an oven. The catalyst silica is reusable and the yields of Chalcones are more than 90%. The structures of the synthesized compounds were confirmed by IR, mass spectroscopy and elemental analysis.

Key words: Chalcone, Claisen-Schmdit condensation, Silica-sulfuric acid IR, Mass and Elemental spectral analysis.

INTRODUCTION

Chalcones are a chemical class that has shown promising therapeutic efficacy for the management of several diseases. Many papers have been presented in the literature with references to structural modifications of the chalcone template[1]. In fact, not many structural templates can claim association with such a diverse range of pharmacological activities, among, which cytotoxicity, antitumour, anti-inflammatory, antiplasmodial, immunosuppression and antioxidant, are widely cited[2].

They considered as the precursor of flavonoids and isoflavonoids. Chemically they consisted of openchain flavonoid by a three carbon, -unsaturated carbonyl system. [3] Recently much attention has been paid on the synthesis of chalcones mainly from acetophenones and aromatic aldehydes by Claisen-Schmidt condensation.

Many reagents and co-ordination complexes of Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) ions with various ligands have been employed for aldol condensation.[4] Metal salts of Cp_2ZrH_2 are used for condensation of cycloalkanones.[5] KF-Al_2O_3 and bis-(*p*-methoxy phenyl) tellurides are have been used for crossed condensation under microwave irradiation.[6] Anhydrous $RuCl_3$ and $TiCl_3$ (SO_3CF_3) have also been applied for aldol condensation reactions under solvent-free conditions.[7]

Now more attention has been paid to synthesis acyclic and cyclic chalcones by chemists.[8] Balakrishna Kalluraya[9] et al. reported 60-70% yield of sydnone chalcones under solvent free condition by aldol condensation reaction by grinding of ketones and aldehydes with sodium hydroxide. Silica-sulfuric acid is used as a versatile and stable solid acid catalyst for organic synthesis.

The promoting effect of silica – sulphuric acid in their reaction was shown good performance and its is proved by obtaining higher percentage of yields. The product was isolated and the remaining catalyst was washed and reused with fresh substrate for further reactions. No decrease in the yield was observed, demonstrating that silica-sulphuric acid can be reused in Claisen-Schmidt condensation reaction without environmental discharge.

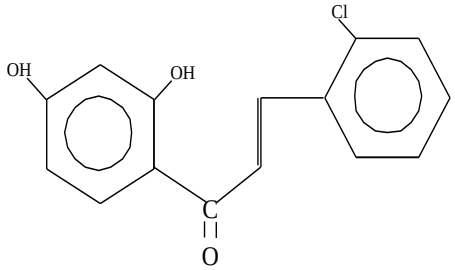
MATERIALS AND METHODS

All the products were synthesized and characterized by their spectral analysis chemicals, 2, 4-dihydroxy acetophenone, 2-chlorobenzaldehydes, 4-chloro benzalde hydes, 3-nitro benzaldehydes, S.D. fine Chemicals (India). Melting points were determined in an open capillary tube and or uncorrected. IR spectra were recorded in KBr on a JASCO FT IR-5300.

The mass spectra were recorded on LCMS-2010 DATA REPORT SHIMADZU. Elemental analysis was carried out on a FLASH EA 1112 SERIES CHN REPORT THERMO FINNIGAN.

Chalcones were synthesized by clasien- Schmidt condensation using Silica Sulfuric acid under solvent free condition. The chemicals and solvents used were of laboratory grade and were purified completion of the reaction was monitored by thin layer chromatography on precoated sheets of silica gel-G (Merck, Germany) using iodine vapour for detection. The synthetic pathway is presented in Scheme 1 and physicochemical data and spectroscopic data for the synthesized compounds are given Table (1-3).

1) Synthesis of 3-(2-chlorophenyl)-1-(2,4-dihydroxyphenyl) prop-2-en-1-one

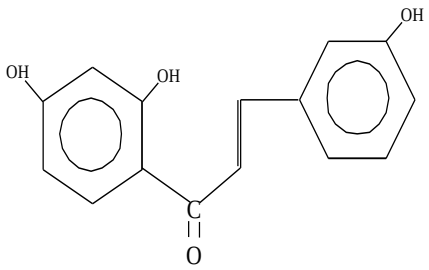


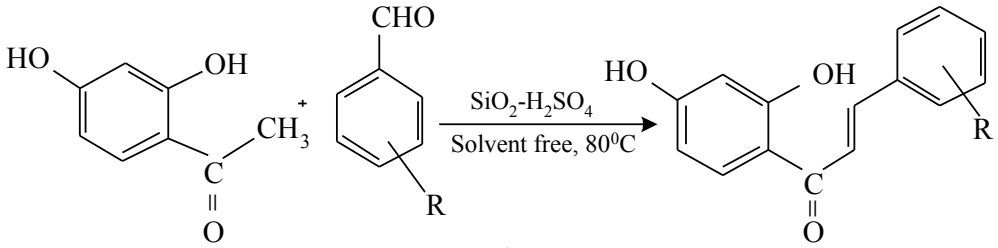
An equimolar mixture of 2,4-hydroxy acetophenone (2gms), aromatic aldehydes (2.1gms) and silica-sulfuric acid (1.5 g equal to 4 mmol of H^+) were mixed thoroughly, place din a glass tube and capped (Scheme 1). The mixture was heated in an oven at 80°CC for 2-3.5h. After complete conversion of the ketones ad monitored by TLC, the mixture was cooled to room temperature. Dichloromethane (20-30ml) was added and heated for 3-5 minutes. The reagent was removed by filtration .

The filtrate was concentrated and the solid residue was recrystallised from ethanol to afford. The catalyst was recycle by washing the solid reagent remained on the filter by ethyl acetate (20 ml) followed by followed by drying in an oven at 50°C for 2h. and can be reusable for another reaction run. Spectral and microanalysis data of selective compounds are summarized below.

2) Synthesis of 1-(2,4-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one

Reaction with 2,4-dihydroxy acetophenone (2 gms) and 4-hydroxy benzal- dehyde (2.1 gm), (2,4-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one was obtained by the above procedure.



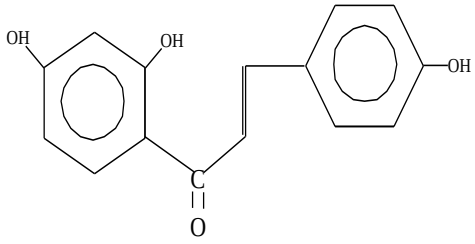


a. R= 2-Cl
b. R= 4-OH
c. R= 3-OH
d. R= 4 NO_2

Scheme -1: Synthetic diagram of 2,4 dihydroxy substituted chalcones

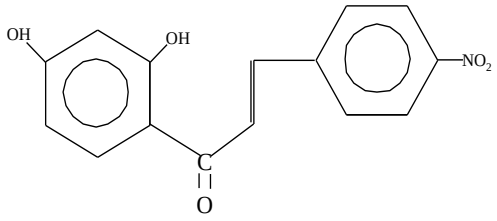
3) Synthesis of 1-(2, 4-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one

A mixture of 2,4-dihydroxy acetophenone (2 gm) add Silica-sulfuric acid under solvent free condition (1.5g) and 3-hydroxy benzaldehyde (2.1 gm); 1-(2-4-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one was obtained by the above procedure.



4)Synthesis of 1-(2,4-dihydroxyphenyl)-3-(4-nitrophenyl)prop-2en-1-one

1-(2,4-dihydroxyphenyl)-3-(4-nitrophenyl)prop-2en-1-one was obtained by the above procedure except that starting material used was 2,4-dihydroxy acetophenone(2.0gm) add Silica-sulfuric acid under solvent free condition (1.5g) and 4 nitro benzaldehyde. (2.2 gm)



RESULTS AND DISCUSSIONS

The Claisen-Schmidt condensation is an important C-C bond formation for the synthesis of 1,3-diaryl-2-propen-1-ones (chalcones). It is generally carried out of the use of strong bases such as Na OH or KOH in polar solvents. The aim of the present study was to develop an efficient and selective protocol for Claisen-Schmidt condensation of 2, 4-dihydroxy condensation and various substuted aldehydes to produced high yield in the presence of a reusable and environmentally beginning catalyst silica-sulphuric acid.

Operative simplicity, easy workup procedure, better yield including washing the mixture followed by evaporation of the solvent is another advantage of this method. Synthesis of chalcone is a single step method. The synthesized chalcone derivatives were undergone physicochemical characterization and the obtained results are given in Table.1. The yields of the synthesized compounds were found to be significant.

The structure of the synthesized compounds was confirmed by IR, Mass and elemental analysis. Elemental analysis showed that the percentage of the nitrogen, hydrogen and carbon was found experimentally is equivalent to the calculated values in all compounds.

All the compounds give the characteristic IR peak that proved that the presence of particular functional group (Table 2) and mass spectroscopy helps to find the molecular weight of the synthesized compounds (Table 3). The Chalcone derivatives showed that the molecular ion peak that equivalent to the molecular weight of proposed compound. Hence m/z value confirms the molecular weight of the respective synthesized compound.

Table -1: Physicochemical characterization data for synthesized compounds

Compound Number	Molecular formula	Molecular weight	Yield (%)	M.P. °C	Elemental analysis		
					C	H	N
1	$C_{15}H_{11}ClO_3$	274	93	176	66.56 (65.75)	4.06 (4.04)	-
2	$C_{15}H_{12}O_4$	256	94	178	70.41 (70.37)	4.65 (4.72)	-
3	$C_{15}H_{12}O_4$	256	91	173	70.48 (70.37)	4.78 (4.72)	-
4	$C_{15}H_{11}NO_5$	285	81	175	63.26 (63.21)	3.85 (3.69)	4.98 (4.91)

Table 2: IR spectral data of synthesized compounds

Compound number	Compound	IR. Spectral data
1	3-(2-chlorophenyl)-1-(2,4-di-hydroxyphenyl)prop-2-en-1-one	IR (KBr) *v* cm^{-1}, (-OH) 3232 cm^{-1},(C=0) 1691 cm^{-1}, (C=C) 1595 cm^{-1}
2	1-(2,4-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one	IR (KBr) *v* cm^{-1}, (-OH) 3177 cm^{-1},(C=0) 1672 cm^{-1}, (C=C) 1633 cm^{-1}
3	1-(2,4 dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one	IR (KBr) *v* cm^{-1}, (-OH) 3194 cm^{-1},(C=0) 1668 cm^{-1}, (C=C)1581 cm^{-1}
4	1-(2,4 dihydroxyphenyl)-3-(4-nitrophenyl)prop-2en-1-one	IR (KBr) *v* cm^{-1}, (-OH) 3113 cm^{-1},(C=0) 1693 cm^{-1}, (C=C)1601 cm^{-1}

Table 3: Mass spectral data of synthesized compounds

Compound number	Compound	Molecular weight	Mass spectral data
1	3-(2-chlorophenyl)-1-(2,4-dihydroxyphenyl) prop-2-en-1-one	274	274 M^{+2}
2	1-(2,4-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one	256	256 $M^{+}H$
3	1-(2, 4-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one	256	256 $M^{\cdot}H$
4	1-(2,4-dihydroxyphenyl)-3-(4-nitrophenyl)prop-2en-1-one	285	285 M^{+}

- 3-(2-chlorophenyl)-1-(2,4-dihydroxyphenyl) prop-2-en-1-one of C_{15} $H_{11}ClO_3$ with molecular ion peak at (274 M^{+2}) showed that m/z is equivalent to molecular weight of proposed compound. Hence m/z value confirms the molecular weight of the compound. The IR peak at 1691 cm^{-1} suggesting the presence of (C=O) group. The IR peak at 1595 cm^{-1} indicates that the presence of (C=C) group. IR peak at 3,232 cm^{-1} indicates presence of (-OH). Melting point of the compound is 176°C which is uncorrected.
- 1-(2,4-dihydroxyphenyl)-3-(4-hydroxyphenyl) prop-2-en-1-one have mole-cular formula C_{15} $H_{12}O_4$ and the molecular weight of the compound is equivalent to the molecular ion peak at (256 $M^{+}H$) of the compound. Hence m/z value confirms the molecular weight of compound. The IR peak at 1672 cm^{-1} suggesting the presence of (C=O) group. The IR peak at 1633 cm^{-1} indicates that the presence of (C=C) group. The IR peak at 3177 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 173 °C which is uncorrected.
- The molecular formula of 1-(2, 4-dihydroxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one is $C_{15}H_{12}O_4$ molecular ion peak at (256 $M^{\cdot}H$) that m/z is equivalent to molecular weight of proposed compound Hence m/z value confirms the molecular weight of compound. The IR peak at 1668 cm^{-1} suggesting the presence of C=O group. The IR peak at 1581 cm^{-1} indicates that the presence of C=C group. IR peak at 3194 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 178 °C which is uncorrected.
- The obtained molecular ion peak of 1-(2,4-dihydroxyphenyl) -3-(4-nitrophenyl) prop-2-en-1-one (molecular formula, ($C_{15}H_{11}NO_5$) at 285 (M^{+}) that m/z is equivalent to molecular weight of proposed compound. Hence m/z value confirms the molecular weight of compound. The IR peak at 1693 cm^{-1} suggesting the presence of (C=O) group. The IR peak at 1601 cm^{-1} indicates that the presence of (C=C) group. IR peak at 3113 cm^{-1} indicates presence of (-OH) group. Melting point of the compound is 175°C which is uncorrected.

CONCLUSION

This method is a very efficient and selective protocol for Claisen-Schmidt condensation of 2,4-dihydroxy Chalcones in the presence of a reusable and environmentally beginning catalyst Silica-sulfuric acid. Operative simplicity, easy work-up procedure, better yield including washing the mixture followed by evaporation of the solvent are other advantages of this method. The reaction was clean and the products were obtained in excellent yields without formation of any side products. The synthesized compounds were characterized by TLC, melting point, IR spectroscopy, elemental analysis and mass spectroscopy. The results obtained form this study confirmed that the product has formed. Henceforth viewing these characteristic properties more compounds can be synthesized and subjected to pharmacological evaluation. These Chalcone derivatives may have variety synthesis and characterization of some new chalcone derivatives.

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